

U.S.S.N. 09/395,409
Cantor, et al.
Preliminary Amendment

91. (New) The method of claim 89, wherein the mass spectrometry comprises a step selected from the group consisting of Fourier Transform, ion cyclotron resonance, time of flight analysis with reflection, time of flight analysis without reflection, and quadrupole analysis, or a combination thereof.

92. (New) The method of claim 89, wherein the mass spectrometry comprises matrix-assisted desorption ionization and time of flight analysis.

93. (New) The method of claim 89, wherein the mass spectrometry comprises electrospray ionization and quadrupole analysis.

94. (New) The method of claim 89, wherein two or more molecular weights are determined simultaneously.

95. (New) The method of claim 88, further comprising enzymatically extending the nucleic acid probes of the target array, wherein the hybridized target nucleic acid serves as a template for forming extended strands.

96. (New) The method of claim 95, wherein the extended strands comprise DNA, RNA, protein nucleic acid (PNA) or combinations thereof.

97. (New) The method of claim 88, wherein the array comprises nucleic acid probes that contain at least one mass-modifying functionality.

98. (New) The method of claim 97, wherein the mass-modifying functionality is coupled to a heterocyclic base, a sugar moiety or a phosphate group.

99. (New) The method of claim 97, wherein the mass-modifying functionality is a chemical moiety that does not interfere with hydrogen bonding for base-pair formation.

100. (New) The method of claim 97, wherein the mass-modifying functionality is a thiol moiety, an alkyl moiety.

101. (New) The method of claim 88, further comprising the step of removing alkali cations.

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102. (New) The method of claim 88, further comprising ligating the hybridized target nucleic acids to the probes.

103. (New) The method of claim 88, wherein the target nucleic acid is obtained from a biological sample or a recombinant source.

104. (New) The method of claim 88, where the target nucleic acid is between about 10 to about 1,000 nucleotides in length.

105. (New) The method of claim 88, where the nucleic acid fragments are between about 10 to about 1,000 nucleotides in length.

106. (New) The method of claim 88, wherein the nucleic acid fragments comprise DNA, RNA, protein nucleic acid (PNA) or combinations thereof.

107. (New) The method of claim 88, wherein the target nucleic acid comprises DNA, RNA, protein nucleic acid (PNA) or modifications or combinations thereof.

108. (New) The method of claim 88, wherein the fragments of nucleic acids comprise greater than about 10^4 different members and each member is between about 10 to about 1,000 nucleotides in length.

109. (New) The method of claim 88, wherein the array comprises a collection of probes with sufficient sequence diversity in the variable regions to hybridize to all of the target sequence with complete or nearly complete discrimination.

110. The method of claim 88, wherein the single-stranded at one terminus and a double-stranded region at the opposite terminus.

111. (New) The method of claim 88, wherein the probes are about 10 to about 1,000 nucleotides in length.

112. (New) The method of claim 88, wherein the probes are about 15 to about 200 nucleotides in length.

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113. (New) The method of claim 88, wherein the probes are about 10 to 50 nucleotides in length.

114. (New) The method of claim 88, wherein the double-stranded portion is about 4 to about 30 nucleotides in length.

115. (New) The method of claim 88, wherein the array of nucleic acid probes is attached to a solid support.

116. (New) The method of claim 115, wherein the solid support is selected from the group consisting of plates, beads, microbeads, whiskers, combs, hybridization chips, membranes, single crystals, ceramics, and self-assembling monolayers.

117. (New) The method of claim 115, wherein each probe is attached to the solid support by a bond selected from the group consisting of covalent bond, electrostatic bond, hydrogen bond, cleavable bond, photocleavable bond, disulfide bond, peptide bond, diester bond and selectively releasable bond, or a combination thereof.

118. (New) The method of claim 117, wherein the cleavable bond is cleaved by a cleaving agent selected from the group consisting of heat, an enzyme, a chemical agent and electromagnetic radiation, or a combination thereof.

119. (New) The method of claim 118, wherein the chemical agent is selected from the group consisting of reducing agents, oxidizing agents and hydrolyzing agents, or a combination thereof.

120. (New) The method of claim 118, wherein the electromagnetic radiation is selected from the group consisting of visible radiation, ultraviolet radiation, and infrared radiation.

121. (New) The method of claim 115, wherein there is a spacer between each probe and the solid support.

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122. (New) The method of claim 121, wherein the spacer is selected from the group consisting of oligopeptides, oligonucleotides, oligopolyamides, oligoethyleneglycerol, oligoacrylamides, and alkyl chains of between about 6 to about 20 carbon atoms, or combinations thereof.

123. (New) The method of claim 115, wherein the solid support comprises a matrix that facilitates volatilization of nucleic acids for molecular weight determination by mass spectrometry.

Please add claims 124-127, which replace claims 78-85 as follows:

124. (New) An array of nucleic acid probes, comprising a collection of probes, wherein:

each probe comprises a single-stranded portion and a double-stranded portion;

each single-stranded portion comprises a variable sequence;

the collection contains 4^R probes, where R is the length of the variable region;

the collection of probes has sufficient sequence diversity in the variable regions to hybridize all of a target sequence with complete or nearly complete discrimination; and

the array is attached to a solid support comprising a matrix material that facilitates the volatilization of nucleic acids for mass spectrometry.

125. (New) An array of nucleic acid probes, comprising a plurality of probes, wherein:

each probe comprises a single-stranded portion comprising a variable sequence;

the array is attached to a solid support comprising a matrix that facilitates the volatilization of nucleic acids for mass spectrometry;

the array comprises a nucleic acid probe having at least one mass-modifying functionality.

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126. (New) An array of nucleic acid probes, comprising a plurality of probes, wherein:

each probe comprises a single-stranded portion comprising a variable sequence;

each of the probes comprises a single-stranded portion and a double-stranded portion; and

the array is attached to a solid support comprising a matrix that facilitates the volatilization of nucleic acids for mass spectrometry.

127. (New) A system, comprising:

a mass spectrometer;

a computer; and

the array of claim 124.

REMARKS

A check (\$777) for the fees for an extension of time (\$445) and excess claims (\$332) accompanies this response. Any fees that may be due in connection with this paper or with this application during its entire pendency may be charged to Deposit Account No. 50-1213. If a Petition for extension of time is required, this paper is to be considered such Petition.

Claims 1-55, 58-60, and 63-77, and 86-127 are pending in the application. Claims 56, 57, 61, 62 and 78-85 are cancelled herein without prejudice or disclaimer. No claims are amended because all claims are patentable over cited art.

Claims 88-123, which are added herein, find basis in the specification as originally filed, particularly claim 56. The added claims recite the element that the probes further comprise a double-stranded region, which element is described throughout the application. Claims 124-127 replace claim 78-85. Thus, no new matter has been added.

The arguments set forth below, apply to claim 88-123, which all depend from claim 56 and ultimately depend from claim 1.